

In re Application of: Dror OFER  
 Serial No.: 10/523,131  
 Filed: January 21, 2005  
 Office Action Mailing Date: June 3, 2008

Examiner: Michael L. BORIN  
 Group Art Unit: 1631  
 Attorney Docket: 35898

**In the Claims:**

1. (Currently Amended) A method of obtaining information about a chemically active area of a target molecule, comprising:

providing a set of compounds comprising a set of substantially rigid chemical gauges, each of said gauges comprising at least one set of three binding points in a substantially rigid triangular configuration;

for each of said gauges, defining at least one ~~providing at least one~~ substantially rigid triangular geometric substructure which represents a set of three binding points, each triangular geometric substructure being defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices;

performing a plurality of assays for measuring an interaction of said target with said gauges, each assay measuring an interaction of said target with at least one of said gauges, thereby obtaining a plurality of assay results; and

analyzing said assay results using a plurality of said triangular geometric substructures to obtain information about said chemically active area,

said set of gauges being selected such that at least 50% of a ~~mathematical-chemical~~ triangle space is spanned by the ~~substantially rigid triangular geometric substructures of said gauges,~~

said triangle space defining all possible 3-point pharmacophores defined by a triplet of distances that form a triangle, each distance being in a range of 2-12 angstrom, and by a triplet of chemical binding point types for the triangle vertices, each chemical binding point type being selected from the group consisting of  
~~, each point in said space being covered by at least 5 distinct gauges from said set;~~

said ~~mathematical-chemical~~ space being defined using a list of at least six chemical binding point types, including acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic, wherein said 3-point pharmacophore represents a set of three binding points on a molecule to which a gauge may bind and  
~~a range of possible distances between chemical binding points including the range of~~

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~~2-12 angstrom, said list and said range defining a space of possible triangular configurations, each configuration including a triplet of distances within said range that form a triangle and a triplet of binding types for the triangle vertices; and~~

a portion of said space being defined as being spanned if there are at least six one substantially rigid triangular substructure available gauges with a substantially rigid triangular configuration of binding points capable of ~~to~~ chemically binding to each 3-point pharmacophore defined by a triangular configuration of binding points selected in said portion of said space;

~~causing said target to interact with a plurality of gauges of said set of gauges;~~

~~assaying said interaction of said gauges with said target to obtain a plurality of assay results; and~~

~~analyzing said assay results to obtain information about said chemically active area.~~

2. (Currently Amended) A method according to claim 1, wherein said set of gauges is selected such that at least 50% of space includes a portion of said triangle space covering the range of distances of between 4 and 8 angstrom, said portion is spanned at least 50%.

3. (Original) A method according to claim 1, wherein said gauges are constructed using a rigid scaffold.

4. (Original) A method according to claim 1, wherein constituent atoms of said gauges do not move more than 1 Å unless at least 20Kcal/Mol are applied to the gauge.

5. (Original) A method according to claim 1, wherein analyzing comprises identifying a plurality of spatial and chemically specific bindings configurations in said target active area.

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6. (Currently Amended) A method according to claim 5, wherein said configurations comprise 3-point pharmacophore~~triangular configurations~~.

7. (Withdrawn-Currently Amended) A method according to claim 5, wherein identifying comprises identifying a 3-point pharmacophore~~configuration~~ that matches a triangular configuration of a bound gauge.

8. (Currently Amended) A method according to claim 5, wherein identifying comprises identifying a 3-point pharmacophore~~configuration~~ that does not match a triangular configuration of a bound gauge.

9. (Original) A method according to claim 8, wherein identifying comprises identifying by statistical analysis of said assay results.

10. (Withdrawn) A method according to claim 9, wherein identifying comprises identifying by clustering.

11. (Withdrawn) A method according to claim 5, wherein identifying comprises assuming each gauge indicates a single configuration.

12. (Withdrawn) A method according to claim 5, wherein identifying comprises assuming at least some of the gauges indicate a plurality of configurations.

13. (Withdrawn) A method according to claim 5, wherein identifying comprises classifying gauges by chemical moieties at vertexes of said configurations.

14. (Currently Amended) A method according to claim 1, comprising reconstructing a spatial map of at least part of said chemically active area, from at

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least two of said assay results, said spatial map~~part~~ including at least four chemical binding areas.

15. (Currently Amended) A method according to claim 14, wherein said spatial map~~part~~ includes at least six chemical binding areas.

16. (Withdrawn-Currently Amended) A method according to claim 5, comprising reconstructing a spatial map of at least part of said chemically active area, from at least two of said configurations, said spatial map~~part~~ including at least four chemical binding points.

17. (Withdrawn-Currently Amended) A method according to claim 16, wherein said spatial map~~part~~ includes at least six chemical binding areas.

18. (Withdrawn) A method according to claim 16, wherein reconstructing comprises:

test-reconstructing a plurality of spatial maps from said configurations;  
scoring said maps; and  
selected a spatial map based on its score.

19. (Withdrawn) A method according to claim 16, wherein reconstructing comprises:

test-reconstructing a plurality of spatial maps from said configurations;  
clustering said maps according to common substructures; and  
selected a spatial map based on a relative property of a cluster it belongs to.

20. (Withdrawn) A method according to claim 19, wherein said relative property comprises size.

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21. (Original) A method according to claim 16, wherein said spatial map includes enough binding points to ensure binding of a small molecule drug having a chemical profile matching the binding points.

22. (Withdrawn) A method according to claim 21, wherein said spatial map includes at least 6 binding points.

23. (Withdrawn) A method according to claim 21, wherein said spatial map includes at least 8 binding points.

24. (Currently Amended) A method according to claim 1, wherein said set of gauges comprises a set of gauges with at least 10,000 distinct gauges.

25. (Currently Amended) A method according to claim 1, wherein said set of gauges comprises a set of gauges with at least 50,000 distinct gauges.

26-28. (Canceled)

29. (Currently Amended) A method according to claim 1, wherein at least 0.5% of said gauges bind with said target when said target is interacted with said gauges.

30. (Currently Amended) A method according to claim 1, wherein at least 1% of said gauges bind with said target when said target is interacted with said gauges.

31. (Currently Amended) A method according to claim 1, wherein at least 3% of said gauges bind with said target when said target is interacted with said gauges.

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32. (Original) A method according to claim 1, wherein at least 50% of said gauges are defined by adding moieties to a set of fewer than 100 scaffolds.

33. (Original) A method according to claim 1, wherein at least 50% of said gauges are defined by adding moieties to a set of fewer than 50 scaffolds.

34. (Currently Amended) A method according to claim 1, wherein ~~at least~~ said set of gauges uses fewer than 15 different chemical moieties to define the chemical behavior of said gauges.

35. (Currently Amended) A method according to claim 1, wherein ~~at least~~ said set of gauges uses fewer than 10 different chemical moieties to define the chemical behavior of said gauges.

36. (Original) A method according to claim 1, wherein said assay is a functional assay.

37. (Withdrawn) A method according to claim 1, wherein said assay is a binding assay.

38. (Withdrawn) A method according to claim 1, wherein said assay is a cellular assay.

39. (Withdrawn) A method according to claim 1, wherein said assay is a flow-through assay.

40. (Original) A method according to claim 36, wherein said functional assay is performed in the presence of a natural substrate of said target.

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41. (Original) A method according to claim 1, wherein said target comprises a protein including a biochemically active area adapted to engage a substrate.

42. (Original) A method according to claim 41, wherein said chemically active area comprises an area including said biochemically active area.

43. (Original) A method according to claim 41, wherein said chemically active area comprises a control area of said protein.

44. (Currently Amended) A method according to claim 1, wherein said analyzing comprises analyzing successful binding of at least 60 distinct gauges.

45. (Currently Amended) A method according to claim 1, wherein said analyzing comprises analyzing successful binding of at least 10 distinct gauges.

46. (Currently Amended) A method according to claim 1, wherein said analyzing comprises analyzing successful binding of at least 100 distinct gauges.

47. (Original) A method according to claim 5, wherein identifying comprises identifying at least 40 different configurations.

48. (Original) A method according to claim 5, wherein identifying comprises identifying at least 10 different configurations.

49. (Original) A method according to claim 5, wherein identifying comprises identifying at least 100 different configurations.

50. (Withdrawn) A method according to claim 16, comprising:  
comparing said map to a lead data base; and

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selecting a lead from said data base for further use responsive to a semblance or lack of semblance between said lead and said map.

51. (Withdrawn) A method according to claim 16, comprising:  
comparing said map to a lead data base; and  
rejecting a lead from said data base for further use responsive to a semblance between said lead and said map.

52. (Withdrawn) A method according to claim 16, comprising:  
constructing a lead to have a semblance to said map.

53. (Withdrawn) A method according to claim 52, wherein constructing comprises constructing using said gauges or scaffolds used to define said gauges.

54. (Original) A method according to claim 5, comprising:  
comparing said configurations to a lead data base; and  
selecting a lead from said data base for further use responsive to a matching of said configurations to said lead.

55. (Original) A method according to claim 5, comprising:  
constructing a lead based on said configurations.

56. (Original) A method according to claim 5, comprising:  
selecting at least one of said gauges as a lead for drug discovery.

57. (Withdrawn) A method according to claim 1, comprising comparing the binding of gauges with similar binding geometries to obtain steric clashing data; and  
analyzing said steric clashing data to provide geometrical information about said target.



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58–101. (Cancelled)

102. (Withdrawn) A method according to claim 1, comprising generating a set of drug leads for said target based on said information.

103. (Withdrawn) A method according to claim 102, comprising removing known drug leads for said target from said set.

104–154. (Cancelled)

155. (Previously Presented) A method according to claim 1, wherein said analyzing comprises characterizing said chemically active area.

156. (Previously Presented) A method according to claim 155, wherein said chemically active area comprises at least two disjoint chemically active areas.

157. (Withdrawn) A method according to claim 1, wherein said analyzing comprises taking said rigidity into account of said analyzing.

158. (Previously Presented) A method according to claim 1, wherein said target molecule comprises an agricultural chemical target.

159. (Previously Presented) A method according to claim 1, wherein said target molecule comprise a drug target.

160. (Canceled)

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161. (Currently Amended) A method according to claim 1, wherein at least 0.1% of said gauges bind with said target when said target is interacted with said gauges.

162. (Currently Amended) A method according to claim 1, wherein said binding points of said gauges~~the moieties~~ comprise Hydroxyl (OH), Carboxyl (COOH), Amide (CONH<sub>2</sub>), Ethyl (CH<sub>2</sub>-CH<sub>3</sub>), Propyl (CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>3</sub>), Phenyl (C<sub>6</sub>H<sub>5</sub>, 6 member aromatic ring).

163. (Previously Presented) A method according to claim 1, wherein said chemically active area comprises at least two disjoint chemically active areas.

164-171. (Cancelled)